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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/546,201	04/10/2000	John M. Polo	PP1463.002	3605
27476	7590	06/20/2005	EXAMINER	
Chiron Corporation Intellectual Property - R440 P.O. Box 8097 Emeryville, CA 94662-8097			FOLEY, SHANON A	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/546,201

Applicant(s)

POLO ET AL.

Examiner

Shanon Foley

Art Unit

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 31 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 31 May 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 26,28-31 and 33-44.

Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

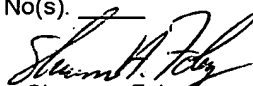
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See the attached correspondence.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s).

13. ☐ Other: _____.


Shanon Foley
Primary Examiner
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Request for Reconsideration

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26, 28-31 and 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky, Jr. et al. (US 6,015,686), which is hereinafter referred to as “Dubensky”, Cella et al. (Journal of Experimental Medicine. March 1, 1999; 189 (5): 821-829), hereinafter “Cella”, Chada et al. (US 5,736,388), hereinafter “Chada” and Gillespie et al. (WO 90/14090), hereinafter “Gillespie” for reasons of record.

Applicant submits that the Office has merely identified the instant individual components taught in the references and does not provide motivation to arrive at the instant expression vectors. More specifically, applicant argues that the teachings of Dubensky and Chada do not arrive at the present invention of expressing multiple genes from different promoters. Applicant argues that neither reference provides motivation to replace one of the multiple heterologous genes of Dubensky and Chada with double stranded, self-complementing RNA.

Applicant's arguments and a review of the references have been fully considered, but are found unpersuasive. Contrary to applicant's assertions, Dubensky and Chada teach expressing multiple heterologous genes from the same construct. Dubensky explicitly teaches that the expression vector is used to express multiple heterologous genes, see column 16, line 61 to column 17, line 29, column 85, line 50 to column 94, line 18, claims 1, 2, 9, 10, column 4, lines

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36-39, column 23, lines 30-36 and column 27, line 60 to column 28, line 2. Chada also teaches a eukaryotic layered vector initiation system that utilizes the same viral vectors and the same promoters of Dubensky, see column 16, line 48 to column 17, line 21. Chada states that one promoter within the same construct may be inadequate to ensure an adequate level of expression of all heterologous genes, see column 26, lines 4-21. This express teaching provides explicit motivation to express multiple heterologous genes of Dubensky from different promoters within the same construct.

Regarding the expression of self-complementing double-stranded (ds) RNA from the vector of Dubensky, applicant is incorrect that there is no motivation to replace dsRNA for one of the multiple genes expressed from the vector of Dubensky because Dubensky already claims a vector construct expressing an antisense sequence or a non-coding sequence, see claim 10. The antisense sequence and the non-coding sequence recited in the claim encompass an antisense RNA that forms double-stranded RNA. Therefore, Dubensky teaches a construct encoding a polymerase II promoter encoding an antigen from a pathogenic agent, as well as a construct encoding a nucleic acid that forms double-stranded RNA for the induction of interferon, see column 23, lines 1-13. Dubensky does not teach dsRNA with self-complementing sequences. However, Gillespie teaches dsRNA with complementing sequences from a vector construct to induce the production of interferon, see page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16. In addition, Cella teaches that double-stranded RNA induces interferon, protects against cytopathic effects of a virus in dendritic cells and increases the capacity of dendritic cells to prime T cells, see the abstract and the first two paragraphs in the discussion section on page 826. Therefore, one of ordinary skill in the art at the time the invention was made would have had

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numerous motivations to induce the production of interferon with the complementary, double-stranded RNA of Gillespie: to protect dendritic cells from viral infection and generate a CTL response to a viral infection, see page 821 and the first two paragraphs in the discussion section on page 826 of Cella and elicit a specific immune response with a viral antigen of Dubensky and induce the production of interferon, taught by Dubensky and Gillespie. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of expressing the dsRNA of Gillespie in the vector of Dubensky to induce interferon because Dubensky, like Gillespie, already expresses dsRNA from a vector to induce the production of interferon, see the previous citations of both references.

Applicant argues that the passage cited in Dubensky does not teach or suggest dsRNA via self-complementation and that there is no motivation to substitute self-complementing dsRNA with the antisense RNA of Dubensky.

Applicant's arguments have been fully considered, but are found unpersuasive. The dsRNA of Dubensky induces the production of interferon, see column 23, lines 1-13. The self-complementing dsRNA of Gillespie also induces the production of interferon, see page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16. Therefore, the dsRNA of Dubensky and the self-complementing dsRNA of Gillespie are *prima facie* obvious alternatives to one another for the induction of interferon.

Applicant also argues that neither Gillespie nor Cella teach *in vivo* transcription of dsRNA from an expression vector. Applicant asserts that Gillespie teaches dsRNA formed *in vitro* and subsequently administered and that Cella teaches nothing with regard to expression vectors and cannot teach the *in vivo* transcription claimed.

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Applicant's arguments and a review of the references have been fully considered, but are found unpersuasive. Cella is not required to teach expression of dsRNA from a vector because Dubensky and Gillespie do. Contrary to applicant's assertion, it is not conclusive that Gillespie does not teach inducing interferon with dsRNA formed *in vivo* since the dsRNA of Gillespie is transcribed in cells from a plasmid vector, see page 5, lines 3-8, 25-29, page 6, lines 5-6 and Figure 3, and the cells could be in tissue culture or in animals, see page 7, lines 16-22. In any case, *in vivo* expression of dsRNA from a vector is taught and claimed by Dubensky, see column 23, lines 1-13 and claims 1, 10 and 18.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the instant case, a difference between the instant invention and the construct of Dubensky is expression of multiple genes from different promoters. However, Chada, which uses the same construct as Dubensky, explicitly teaches using multiple promoters within the same construct to ensure an adequate level of expression of all heterologous genes, see column 26, lines 4-21. Therefore, one of ordinary skill is not only provided with the requisite motivation to use more than one promoter in the construct of Dubensky, but also a reasonable expectation of

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success for doing so because Dubensky teaches expressing multiple genes and Chada teaches using the same expression construct as Dubensky.

The second difference between the construct of Dubensky and the instant claims is the expression of self-complementing dsRNA. However, Gillespie teaches dsRNA with complementing sequences from a vector construct to induce the production of interferon, see page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16. Since the dsRNA of Dubensky and the dsRNA of Gillespie both induce the production of interferon, they would have been prima facie obvious alternatives to one another to one of ordinary skill, absent unexpected results to the contrary. Further, the ordinary artisan would have had several motivations from the references themselves to express the self-complementing dsRNA of Gillespie in the construct of Dubensky. These motivations include inducing the production of interferon (see page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16 of Gillespie), inducing interferon, protecting against cytopathic effects of a virus in dendritic cells and increasing the capacity of dendritic cells to prime T cells (see the abstract and the first two paragraphs in the discussion section on page 826 of Cella), and finally, inducing the production of interferon and eliciting a specific immune response against a viral antigen (see the previous citations of Dubensky). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for expressing the dsRNA of Gillespie in the vector of Dubensky to induce interferon because Dubensky, like Gillespie, already express dsRNA from a vector to induce the production of interferon, see the previous citations of both references.

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Therefore, it is maintained that the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Shanon Foley
Primary Examiner
Art Unit 1648